

The association between ambient temperature and childhood asthma: a systematic review

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Received: 5 May 2017 / Revised: 18 September 2017 / Accepted: 24 September 2017
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Abstract The objectives of this study are to review available information on the association between ambient temperature and childhood asthma, and to elucidate the possible underlying mechanisms of this relationship. A systematic review was conducted based on the papers retrieved from four databases, including PubMed, ProQuest, ScienceDirect, and Scopus. Papers examining the association of absolute temperature or temperature variation with childhood asthma published from 1 January 2000 to 31 December 2016 were included. Thirteen papers have quantified the effect of absolute temperature on childhood asthma, and six papers have examined the effect of intra- or inter-day temperature variation on childhood asthma. All studies were conducted in urban areas. Aeroallergen sensitizations were only considered in the analyses of one study. Discrepancy existed in the significance of the relationship between absolute temperature and childhood asthma, and also in the shape of this relationship (i.e. linear or non-linear)

and whether temperature effects were lagged. Increasing evidence is suggesting non-linear relationship between absolute temperature and childhood asthma. Future research should investigate the burden of childhood asthma specifically attributable to extreme temperatures and temperature variation using advanced statistical approach, particularly in rural areas, after properly considering aeroallergens and air pollution. Projecting future burden of childhood asthma under climate change scenarios is also warranted.

Keywords Absolute temperature · Aeroallergen · Air pollution · Childhood asthma · Temperature variation

Introduction

Asthma, one of the most common chronic diseases, has caused a substantial burden of disease worldwide (Kassebaum et al. 2016), especially in children (Asher and Pearce 2014). As asthma is not curable, identifying its risk factors and developing tailored intervention strategies are crucial for asthma control and prevention (Beasley et al. 2015). Genetic (Ding et al. 2013) and environmental factors (Ahluwalia and Matsui 2011; Gern 2010), as well as the gene-environment interactions (Forno et al. 2017; Gref et al. 2017), are largely associated with the occurrence of childhood asthma.

Recent literature has well documented the association between exposure to outdoor air pollution and the onset of childhood asthma (Khreis et al. 2017). The effect of ambient temperature on the occurrence of childhood asthma has also attracted increasing concern from scientists and the public (Xu et al. 2013a; Lam et al. 2016), especially under the context of climate change (D'Amato et al. 2014). Cold temperature may trigger childhood asthma as airway

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cooling in cold days may exacerbate inflammation which causes a narrowing of airways (Kaminsky et al. 2000), and high temperature may increase the occurrence of childhood asthma by enhancing the growth of indoor allergens such as mites and cockroaches (Hashimoto et al. 2004).

As climate change progresses, global surface temperature will increase (IPCC 2013), and the duration, frequency, and intensity of persistent hot days (i.e. heatwave) will also increase (Meehl and Tebaldi 2004), suggesting the possibility of increasing childhood asthma attributable to high temperature, although cold-related burden of childhood asthma might be reduced. As such, comprehensive evaluation of the available data on the association between ambient temperature and childhood asthma is needed. This study aimed to systematically review existing studies concerning the association between ambient temperature (absolute temperature and temperature variation) and childhood asthma, and to summarize/elucidate the possible pathways through which ambient temperature may affect childhood asthma. This review has also identified the knowledge gaps in previous studies and proposed solutions accordingly, calling for more research attention to be paid to this area given the fact that climate is changing and childhood asthma burden is considerable globally.

Materials and methods

Data sources

This systematic review was conducted according to PRISMA guidelines (Moher et al. 2015). Four databases, including PubMed, ProQuest, ScienceDirect, and Scopus, were used to retrieve papers examining the short-term effects of absolute temperature and intra- or inter-day temperature variation on childhood asthma which were published between 1 January 2000 and 31 December 2016. The references of the included papers were manually checked to make sure all studies were included. Children were defined as those aged under 18 years.

Inclusion criteria

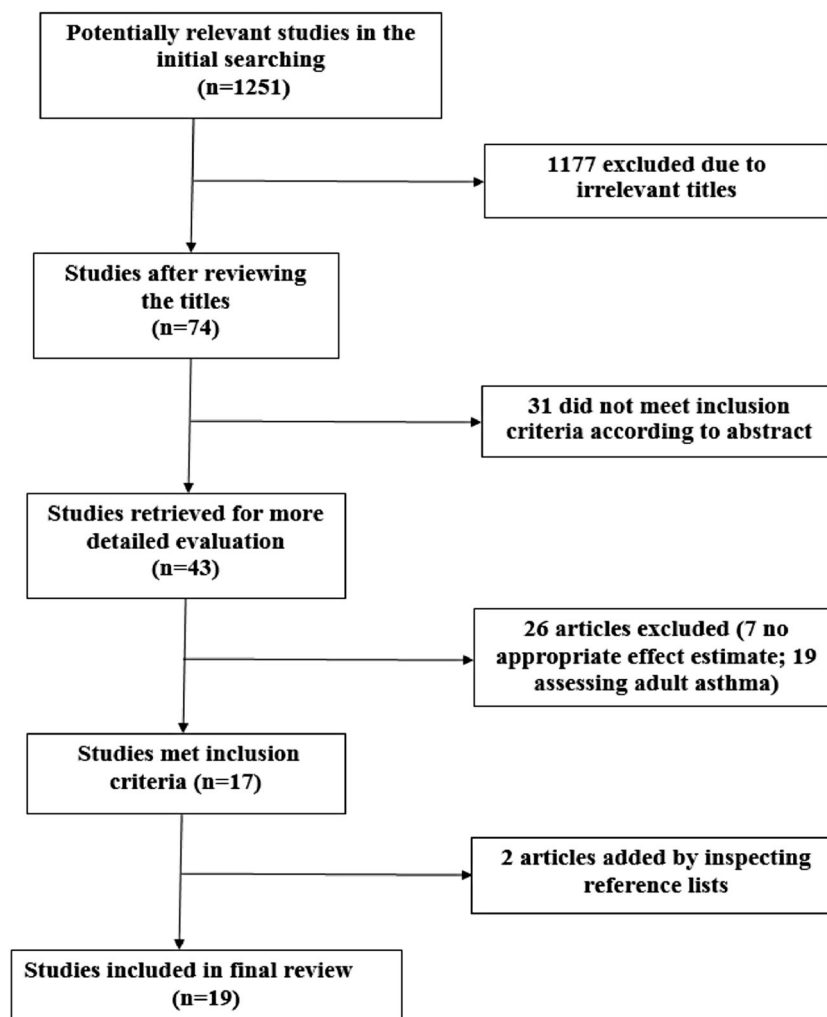
The following U.S. National Library of Medicine's Medical Subject Headings (MeSH terms) and keywords in the initial search: 'climate change', 'temperature', 'temperature variability', 'temperature variation', 'temperature change', and 'asthma'. The inclusion criteria is empirical studies using original data and appropriate effect estimates (e.g. coefficient, relative risk, and odds ratio, etc.) where ambient temperature was a main exposure of interest, and where the short-term effect of absolute temperature or temperature change on childhood asthma was analysed.

Results and discussion

Initially, 1251 papers were retrieved in the search, and 1234 papers were excluded for a variety of reasons, including irrelevant titles (1177), irrelevant abstracts (31), no appropriate effect estimate (7), and no appropriate age group investigated (19). Seventeen papers fulfilled the selection criteria. Two papers were identified from the references of the selected papers, and therefore 19 papers were included in the final analysis (Fig. 1). Among these 19 papers, 13 assessed the short-term effect of absolute temperature on childhood asthma (Table 1), and 6 examined the short-term effect of intra- or inter-day temperature variation on childhood asthma (Li et al. 2014b, 2016; Mireku et al. 2009; Qiu et al. 2015; Ueda et al. 2010; Xu et al. 2013b) (Table 2). These studies differed in specific age groups included, health outcomes adopted, or effect estimates used, which restricted us from meta analysing the results. Among those studies which examined the effect of absolute temperature on childhood asthma, 1 study focused on low temperature (Guo et al. 2012), 2 focused on high temperature (Soneja et al. 2016; Winquist et al. 2016), and the other 10 studies focused on a spectrum of temperature values (Abe et al. 2009; Hashimoto et al. 2004; Hervás et al. 2015; Lam et al. 2016; Li et al. 2014a; Nastos et al. 2008; Son et al. 2014; Xirasagar et al. 2006; Xu et al. 2013a; Yamazaki et al. 2013). The spatial distribution of all included studies was presented in Fig. 2.

High temperature and childhood asthma

Among all 12 studies which examined the effects of 'heat' or 'both heat and cold' on childhood asthma, eight studies have found a significant effect of heat on childhood asthma (Hashimoto et al. 2004; Lam et al. 2016; Li et al. 2014a; Son et al. 2014; Soneja et al. 2016; Winquist et al. 2016; Xu et al. 2013a; Yamazaki et al. 2013). This discrepancy may be due to the differences in climates, socioeconomic statuses, or statistical methods used in these studies. Four analytical approaches were mainly used in these 12 studies, including linear regression (Hashimoto et al. 2004; Hervás et al. 2015; Nastos et al. 2008), generalized linear/additive regression allowing for a possible non-linear relationship between temperature and asthma (e.g. using splines to smooth temperature) (Lam et al. 2016; Son et al. 2014; Winquist et al. 2016; Xu et al. 2013a), autoregressive integrated moving average model (ARIMA) (Abe et al. 2009; Xirasagar et al. 2006), and case-crossover analysis (Soneja et al. 2016; Yamazaki et al. 2013). As the possible effect of ambient high/low temperature on childhood asthma may not occur immediately after exposure, and both high and low temperatures may affect childhood asthma, we argue that it might be judicious to investigate the linearity of this temperature-asthma relationship and to test how long this effect may last (Michelozzi et al. 2009) before confirming the analytical strategy.

Fig. 1 The flow chart of literature selection process

Ambient temperature affects the occurrence of childhood asthma directly through acting on airways and changing the pattern of human behaviours, and indirectly through influencing airborne allergens and pollutant levels (D'Amato and Cecchi 2008). Existing evidence on the underlying mechanisms includes three aspects. Firstly, high temperature activates vagal bronchopulmonary C-fiber sensory nerves, which upon activation can elicit reflex bronchoconstriction (Don Hayes et al. 2012). Secondly, high temperature can enhance the growth of and exposure to indoor aeroallergens, such as mould spores and cockroaches (Hashimoto et al. 2004). Thirdly, the level of air pollutants (e.g. ozone) may be higher on hot days (Ebi and McGregor 2008), and the high level of air pollution may directly trigger the occurrence of childhood asthma (Weinmayr et al. 2010) or indirectly affect childhood asthma by increasing the effect of aeroallergens on childhood asthma (Cakmak et al. 2012).

Low temperature and childhood asthma

Compared with high temperature, low temperature has been widely recognized as a trigger/risk factor for childhood

asthma for a longer time. Eleven studies have examined the effect of low temperature on childhood asthma, and seven of them have found a significant result (Guo et al. 2012; Hervás et al. 2015; Lam et al. 2016; Nastos et al. 2008; Son et al. 2014; Xirasagar et al. 2006; Xu et al. 2013a). One note-worthy study which was conducted in Shanghai (a humid subtropical city), China, assessed the effect of persistent cold days (i.e. cold spells) on childhood asthma, and found that a lower temperature corresponded to a higher risk of asthma attack (Guo et al. 2012), indicating that persistent cold may pose some additional threat to asthmatic children. However, this finding was not observed in Brisbane, Australia (Xu et al. 2013a), which also has a subtropical climate.

Several pathways through which low temperature affects the occurrence of childhood asthma have been proposed in the existing literature. Firstly, low temperature is associated with decreasing lung function and lower lung capacity (Koskela et al. 1994). Secondly, low temperature has significant effects on suppressing the immune system of human being (LaVoy et al. 2011). Thirdly, low temperature facilitates the transmission and survival of respiratory virus (Hashimoto et al. 2004)

Table 1 Characteristics of included studies regarding the short-term effect of absolute temperature on childhood asthma

Authors and year of publication	Population	Definitions of high and low temperatures	Outcome investigated	Location and period of data obtained	Climate of the study site	Temperature measure(s)	Analytical approach	Study objective	Key findings
Hashimoto et al. 2004	2–15 years	Not mentioned	Hospitalizations for asthma	Tokyo, Japan, 1998–2002	Temperate	Daily mean and maximum temperatures	Multiple logistic regression	Examine the associations of climate variables (e.g. temperature, barometric pressure, relative humidity and wind speed, etc.) with childhood asthma	High daily mean temperature was associated with the increase in hospitalizations in childhood asthma (coefficient = 0.82, $P < 0.001$)
Xirasagar et al. 2006	0–14 years	Not mentioned	Hospitalizations for asthma	Taiwan, 1998–2001	Subtropical to tropical	Monthly mean temperature	Correlation analysis	Examine the associations of climate variables (temperature, relative humidity, atmospheric pressure, rainfall and sunshine hours) with childhood asthma	Hospitalizations for asthma were negatively correlated with mean temperature ($r = -0.353$, $P < 0.05$)
Nastos et al. 2008	0–14 years	Not mentioned	Hospitalizations for asthma	Athens, Greece, 1978–2000	Temperate	Daily air temperature	Poisson GLM	Examine the associations of climate variables (air temperature, relative humidity, absolute humidity, and wind speed) with childhood asthma	A decrease of 10 °C in air temperature corresponded to a 31% increase of hospitalizations for asthma in children aged 0–4 years
Abe et al. 2009	0–14 years	Not mentioned	Emergency department visits for asthma	Tokyo, Japan, January to December, 2005	Temperate	Daily minimum temperature	ARIMA model	Examine the associations of climate variables (temperature, barometric pressure, relative humidity and precipitation) with asthma	No significant relationship was found between minimum temperature and emergency department visits for asthma in children
Guo et al. 2012	Not mentioned	Cold: 5th percentile of mean temperature	Outpatients for childhood asthma	Shanghai, China, 2007–2009	Subtropical	Mean temperature	Quasi-Poisson regression	Examine the association between cold spell and childhood asthma	There was a significant relationship between cold temperatures and paediatric outpatient visits for asthma, and at lag 7–14 days,

Table 1 (continued)

Authors and year of publication	Population	Definitions of high and low temperatures	Outcome investigated	Location and period of data obtained	Climate of the study site	Temperature measure(s)	Analytical approach	Study objective	Key findings
Xu et al. 2013a, b	0–14 years	Heat: 95th percentile of mean temperature; Cold: 5th percentile of mean temperatures	Emergency department admissions for asthma	Brisbane, Australia, 2003–2009	Subtropical	Daily mean temperature	Poisson GLM combined with DLNM	Examine the associations of high and low temperatures with childhood asthma	the relative risk was 1.12 (95% CI 1.02, 1.25) Both high and low temperatures were associated with increase in emergency department admissions for asthma, and the relative risks at lag 0–1 days for heat and cold were 1.12 (95% CI 1.02, 1.22) and 1.45 (95% CI 1.20, 1.74), respectively High temperature in summer was associated with increase in primary care visits for asthma (OR = 1.31)
Yamazaki et al. 2013	0–14 years	Not mentioned	Primary care visits for asthma	Himeji City, Japan, April 2010 to March 2012	Subtropical	Daily mean temperature	Case-crossover study, conditional logistic regression	Examine the associations of climate variables (temperature, atmospheric pressure, relative humidity, wind speed, and daylight hours) with childhood asthma	
Li et al. 2014a, b	7–12 years	Not mentioned	Asthmatic symptoms	Six cities of Australia, 2007–2008	Various types of climate	Daily mean temperature	Panel study, mixed logistic regression	Examine the association between ambient temperature and asthmatic symptoms in children	Increasing temperatures induced the risks of children's asthmatic symptoms, especially for "wheeze/chest tightness" and to a lesser extent for "cough/phlegm". The effects were acute and lasted for 4 days
Son et al. 2014	0–14 years	Heat: 25 °C; Cold: 5 °C	Hospital admissions for asthma	Eight cities of Korea, 2003–2008	Various types of climate	Daily mean temperature	Time series, two-stage hierarchical modeling	Examine the associations of heat, cold, and heatwaves with certain cause-specific hospital admissions	Heat and cold effects on asthma were greater in children (0–14 years) than older groups (exact value not shown in the paper)
Hervás et al. 2015	5–14 years	Not mentioned	Emergency department visits for asthma	The island of Mallorca, Spain, 2007–2011	Temperate	Monthly mean temperature	Multiple linear regression	Examine the associations of a range of climate variables with childhood asthma	Mean temperature was positively associated with emergency department visits for childhood asthma (coefficient = 27.2, $P < 0.0001$)

Table 1 (continued)

Authors and year of publication	Population	Definitions of high and low temperatures	Outcome investigated	Location and period of data obtained	Climate of the study site	Temperature measure(s)	Analytical approach	Study objective	Key findings
Lam et al. 2016	0–14 years	Heat: 30 °C; Cold: 12 °C	Hospital admission for asthma	Hong Kong, China, 2004–2011	Subtropical	Daily mean temperature	Poisson GAM combined with DLNM	Examine the association between ambient temperature and childhood asthma	Both high (RR: 1.19 (95% CI 1.06, 1.34)) and low (RR: 1.33 (95% CI 1.13, 1.58)) temperatures were associated with increases in hospital admissions for asthma, and children aged 5–14 years were more sensitive to temperature effects
Soneja et al. 2016	0–17 years	Heat: 95th percentile of maximum temperature	Hospitalizations for asthma	Maryland, US, 2000–2012	Subtropical	Daily maximum temperature	Case-crossover study, conditional logistic regression	Examine the associations of extreme heat and precipitation with asthma	Occurrence of extreme heat events in Maryland increased the risk of same day hospitalization for asthma (OR 1.03, 95% CI 1.00, 1.07), especially for the population aged 5–17 years
Winquist et al. 2016	0–18 years	Heat: 75th percentile of maximum temperature	Emergency department visits for asthma/wheeze	Atlanta, US, 1993–2012	Subtropical	Daily maximum temperature	Quasi-Poisson GLM	Examine the association between warm temperature and cause-specific emergency department visits	An increase of 5 °C in maximum temperature was associated with a 5.9% increase in emergency department visits for asthma in children aged 5–18 years

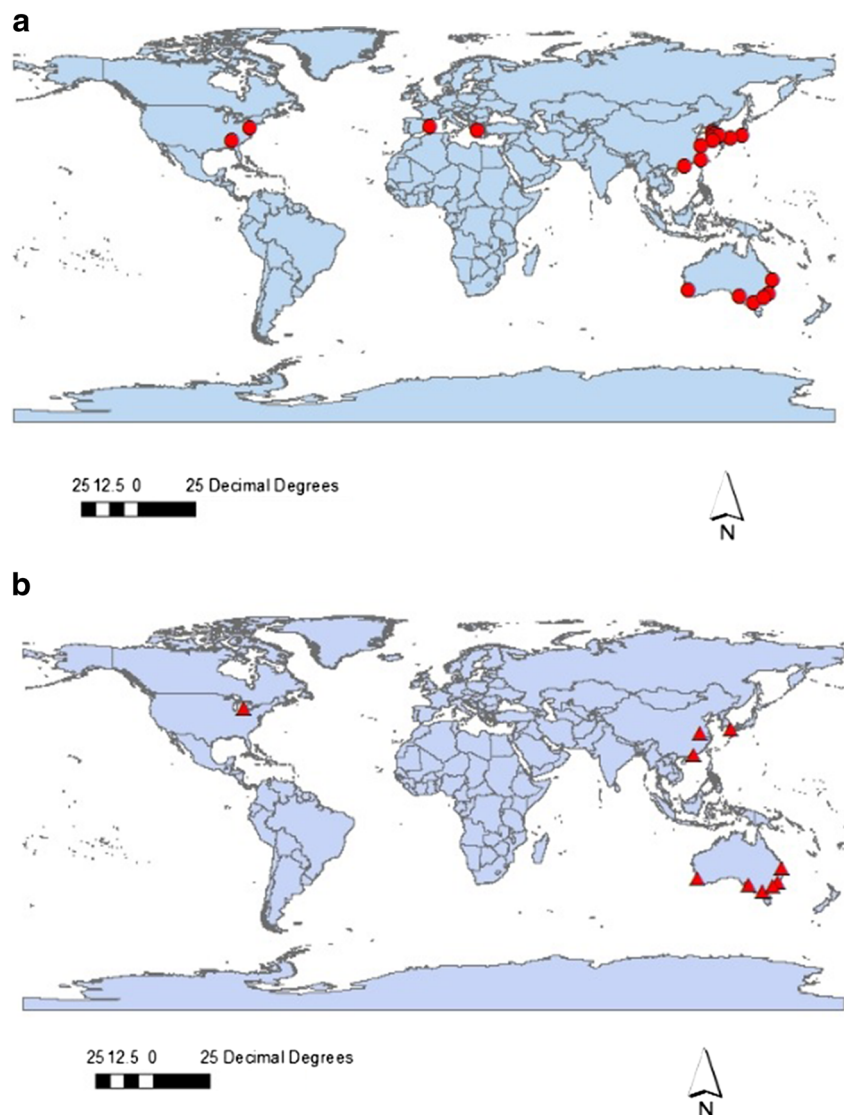
ARIMA, autoregressive integrated moving average model; *CI*, confidence interval; *DLNM*, distributed lag non-linear model; *GAM*, generalized additive model; *GLM*, generalized linear model; *OR*, odds ratio; *RR*, relative risk

Table 2 Characteristics of included studies regarding the effect of intra- and inter-day temperature change on childhood asthma

Authors and year of publication	Population	Outcome investigated	Location and period of data obtained	Climate of the study site	Temperature measure(s)	Analytical approach	Study objective	Key findings
Li et al. 2014a, b	7–12 years	Lung function and respiratory symptoms of asthmatic children	Five large cities of Australia, 2007–2008	Various types of climate	DTR	GAMM	Investigate the association between DTR and asthmatic symptoms in children	An increase in DTR induced a reduction in peak expiratory flow and increased the occurrence of respiratory symptoms. In general, the effects lasted for 3 days
Xu et al. 2013a, b	0–14 years	Emergency department admissions for asthma	Brisbane, Australia, 2003–2009	Subtropical	DTR	Poisson GLM with DLNM	Investigate the association between DTR and childhood asthma	There was a statistically significant relationship between DTR and childhood asthma (relative risk (RR): 1.31, 95% confidence interval (CI): 1.11, 1.58). The DTR effect on childhood asthma increased above a DTR of 10 °C
Mireku et al. 2009	1–18 years	Emergency department admissions for asthma	Detroit, US, 2004–2005	Humid continental climate	DTR and inter-day temperature change	GAM	Investigate the associations of intra- and inter-day temperature change with childhood asthma exacerbation	No significant relationship was found between diurnal temperature range and childhood asthma, but there was a significant relationship between inter-day temperature change and childhood asthma
Ueda et al. 2010	Children under 12 years	Emergency hospitalization for asthma	Fukuoka, Japan, 2001–2007	Temperate	DTR	Case-crossover analysis	Investigate the associations of absolute temperature and temperature change with childhood asthma	The ORs per 1 °C within-day drop and rise during the period from the hospitalizations for asthma day to 3 days previously (lag3) were 1.033 and 1.027
Qiu et al. 2015	0–14 years	Emergency hospital admissions for asthma	Hong Kong, China, 2004–2011	Subtropical	DTR	Poisson GAM with DLNM	Investigate the association between DTR and emergency hospital admissions for asthma	An increment of 1 °C in DTR over lag2 days was associated with a 2.42% (95% CI 0.53%, 4.32%) increase in daily emergency asthma hospitalizations in female children
Li et al. 2016	0–14 years	Hospital visits for asthma	Hefei, China, 2010–2013	Temperate	Inter-day temperature change	Poisson GLM with DLNM	Investigate the associations of intra- and inter-day temperature change with childhood asthma	A 1 °C increase in inter-day temperature change was associated with a 4.2% (95% confidence interval 0.9–7.6%) increase in hospital visits for childhood asthma

DLNM, distributed lag non-linear model; DTR, diurnal temperature range; GAM, generalized additive model; GAMM, generalized additive mixed model; GLM, generalized linear model

Fig. 2 **a** Absolute temperature and childhood asthma. **b** Temperature variation and childhood asthma



and increases the inflammation of airway and thus causes a narrowing of airways and exacerbation of asthma (Donaldson et al. 1999). Fourthly, cold temperature can produce robust increases in intracellular Ca^{2+} levels, but can also increase the expression of MUC5AC mRNA as well as intracellular and secreted MUC5AC protein. This mucin protein may activate transient receptor potential melastatin 8 (TRPM8) and trigger exacerbations of childhood asthma (Li et al. 2011).

Temperature variation and childhood asthma

Apart from extreme temperatures, fluctuation in temperature has also been commonly identified by asthmatic patients as a major trigger of asthma attack (Mireku et al. 2009). Six studies have assessed the effect of intra- or inter-day temperature variation on childhood asthma. Mireku et al. (2009) and Li et al. (2016) have observed a significant relationship between inter-day temperature variation and childhood asthma in Detroit,

USA, and Hefei, China, respectively. Three other studies conducted in Brisbane (Australia) (Xu et al. 2013a), Fukuoka (Japan) (Ueda et al. 2010), and Hong Kong (China) (Qiu et al. 2015) have found that a large intra-day temperature variation (i.e. diurnal temperature range (DTR)) increased the occurrence of childhood asthma. Li et al. (2014a) have investigated the effects of DTR on lung function and respiratory symptoms in asthmatic children and found that an increase in DTR induced a reduction in peak expiratory flow and increased respiratory symptoms, suggesting a possible pathway through which large DTR triggers the occurrence of childhood asthma. There are also two other plausible biological mechanisms of temperature variation impact on childhood asthma. Firstly, sudden change in the temperature of inhaled air has been found to be associated with the release of inflammatory mediators by mast cells (Togias et al. 1985). Graudenz et al. (2006) have observed that sudden temperature changes caused more inflammatory nasal responses in allergic

rhinitis patients. Secondly, weather change may affect humoral or cellular immunity (Bull 1980).

Research gaps and proposed solutions

Although increasing number of studies have investigated the impact of ambient temperature on childhood asthma outcomes (e.g. presentations, admissions, lung function), there are still several knowledge gaps which need to be properly filled. Firstly, what are ‘high temperature’ and ‘low temperature’ has not been well clarified in some previous studies examining the effect of absolute temperature on childhood asthma because some studies focused on a spectrum of temperature values rather than just heat and cold. However, to understand whether childhood asthma occur more in hotter temperatures or colder temperatures, it is ideal to have concrete definitions of ‘high temperature’ and ‘low temperature’ in future studies. Secondly, prior studies concerning the impact of absolute temperature on childhood asthma did not control for aeroallergens (e.g. pollen), and only one study looking at the impact of temperature variation on childhood asthma has controlled for aeroallergen (Mireku et al. 2009), which may partially be attributable to the difficulty in collection of data on aeroallergen exposure and patient sensitization to aeroallergens. Not properly considering aeroallergen factors when assessing the relationship between temperature and asthma may cause bias (Erbas et al. 2016) as aeroallergens may play as a mediator or confounder between weather and asthma. Pollens are specific to local environment. Identifying the primary pollen which triggers childhood asthma and taking exposure to these pollens into account in the data analysis may better quantify temperature effect on childhood asthma. Thirdly, air pollution plays an important role in the occurrence of childhood asthma (Mölter et al. 2015). Exposure to air pollutants may confound or modify the effect of temperature on asthma outcomes (Mirabelli et al. 2016; Ren et al. 2006). Understanding whether air pollutants and temperature work independently or interactively/jointly in triggering the occurrence of childhood asthma is essential for not just better unveiling how temperature may affect childhood asthma but also more adequately understanding the relative roles air pollutants and temperature play in driving the burden of childhood asthma in the future, especially under the context of climate change. Fourthly, cold temperature is associated with the increasing occurrence of influenza in children (Lowen et al. 2007) and consequently may cause asthma hospitalizations (Morales-Suárez-Varela et al. 2017), and thus influenza should be considered when quantifying the effect of temperature on childhood asthma. In Northern Hemisphere, children return to schools in September and this season may also see a spike of increase in hospitalizations for childhood asthma (Johnston et al. 1996). Therefore, school terms also need to be well considered in the assessment of temperature effect on childhood asthma.

Fifthly, existing studies have separately looked at how absolute temperature or temperature variation may affect childhood asthma, but how much proportion of childhood asthma can be specifically attributable to extreme temperatures or temperature variation is still under-researched. Gasparrini and Leone (2014) have proposed an approach to quantitatively measure the attributable burden to particular environmental hazards. Sixthly, all studies examining temperature effect on childhood asthma were conducted in urban areas of high or high-middle income countries/regions, and children living in rural areas, especially in those socioeconomically disadvantaged areas, may have less capacity to adapt to the impacts of extreme temperatures and big temperature variation. Elucidating the possible heterogeneity across urban and rural areas in terms of asthmatic children’s vulnerability to extreme temperatures or big temperature variation, and identifying the drivers behind this heterogeneity, will be beneficial for the development of future tailored intervention strategies. More attention should also been paid to regions from developing countries, especially those in Africa, South Asia, Southeast Asia, the Middle East, or Latin America. Seventhly, climate change is unequivocal, and it will affect the burden of childhood asthma (D’Amato et al., 2016; Beggs and Bambrick 2005). Projecting future burden of childhood asthma under climate change scenarios is warranted as it can provide useful information to policy makers for future allocation of health resources in controlling childhood asthma (Sheffield et al. 2011).

Conclusions

One major goal of childhood asthma management is to control asthma exacerbation, which requires a good understanding of environmental factors that trigger asthma. Future research is needed to quantify the burden of childhood asthma specifically attributable to extreme temperatures and temperature variation using advanced statistical approach, particularly in rural areas, after properly considering aeroallergens and air pollution. Studies projecting future burden of childhood asthma under climate change scenarios are also warranted.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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